Radiographic Progression of Structural Joint Damage in Patients With Active Psoriatic Arthritis Treated With Ixekizumab Over 52 Weeks

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SYNOPSIS

- Ixekizumab is a high-affinity monoclonal antibody that selectively targets interleukin-17A[1]
- Ixekizumab was superior to placebo in achieving clinical responses and inhibiting progression of structural joint damage in patients with psoriatic arthritis treated for 24 weeks[2]
  - The efficacy of ixekizumab in providing persistence of clinical responses through 52 weeks of treatment has been shown in SPIRIT-P1[3,4]

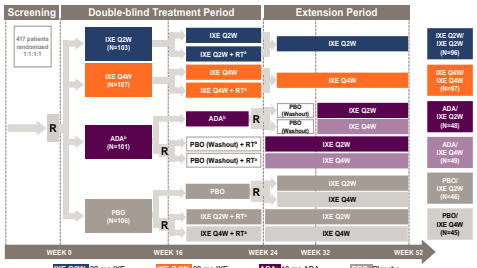
OBJECTIVE

- To assess the impact of ixekizumab on the progression of structural joint damage in patients with psoriatic arthritis who were treated for up to 52 weeks in SPIRIT-P1

METHODS

Study Design

SPIRIT-P1



All IXE patients (starting IXE at Weeks 0, 16, or 24) received a 160-mg starting dose (as two 80 mg injections) followed by 80 mg Q2W or Q4W; Criteria for defining inadequate responders were blinded to investigators
[a] Plus rescue therapy (RT) in inadequate responders; [b] Active reference arm
ADA=adalimumab; IXE=ixekizumab; PBO=placebo; R=randomization; RT=rescue therapy

Key Eligibility Criteria

Inclusion Criteria

- Male or female ≥18-years-old
- Established diagnosis of active psoriatic arthritis ≥6 months and currently meets the CASPAR
- Active psoriatic arthritis defined as the presence of ≥3 tender and ≥3 swollen joints
- ≥1 joint erosion on hand or foot x-rays OR a C-reactive protein concentration >6 mg/L at screening
  - Joint erosions were assessed by central reading
- Active psoriatic skin lesion or a documented history of plaque psoriasis

Exclusion Criteria

- Current or prior use of biologic agents for treatment of psoriasis or psoriatic arthritis
- Inadequate response to ≥4 cDMARDs
- Current use (at study entry) of >1 cDMARD
- Serious infection within 3 months prior to randomization

CASPAR=Classification Criteria for Psoriatic Arthritis; cDMARD=conventional disease-modifying antirheumatic drug

Assessment of Structural Joint Damage

- Assessed using the van der Heijde modified Total Sharp Score (mTSS)
  - Quantifies the extent of bone erosions (20 locations per hand/wrist, 12 locations per foot) and joint space narrowing (20 locations per hand/wrist, 6 locations per foot)
  - Total mTSS score is the sum of bone erosion and joint space narrowing scores
    - Scores range from 0 to 528
    - Higher scores represent greater damage
- X-rays at Weeks 0, 24, and 52 were scored independently by two readers blinded to timepoint and clinical data
  - mTSS scores represent the average score of the two readers

Statistical Analysis

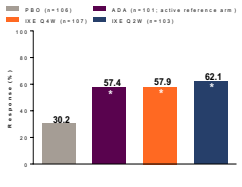
- Extension period population
  - All patients who entered the extension period and received ≥1 dose of study medication during this period
- Prespecified analysis
  - mTSS data were excluded if the radiograph was taken after the scheduled visit date
    - Presented as mean change from baseline to Week 52
- Post hoc analysis
  - mTSS data from radiographs taken after the scheduled visit date were interpolated
    - Presented as mean change from baseline to Week 52
  - Cumulative probability plots were created to visualize patient-level data
  - Summaries are presented for the proportion of patients with no radiographic progression, defined as the mTSS change from baseline to Week 52 ≤ cut-off values of: 0.0, 0.5, and 1.32 (the smallest detectable change from baseline to Week 52 in this study)
- Missing data were imputed using linear extrapolation method if ≥1 postbaseline value was available

mTSS=van der Heijde modified Total Sharp Score

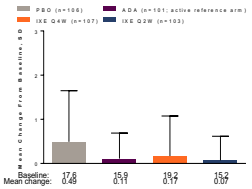
RESULTS

Week 24: ACR20 Response Rate and mTSS Change From Baseline[1]

ACR20 Response Rate at Week 24, NRI, ITT Population



mTSS Change From Baseline to Week 24, Linear Extrapolation, ITT Population



* p<.001 vs. placebo (ACR20, logistic regression analysis; mTSS, ANCOVA)
ACR20=American College of Rheumatology 20% response; ADA=40 mg adalimumab every 2 weeks (active reference arm); ANCOVA=analysis of covariance; IXE Q2W=80 ixekizumab every 2 weeks; IXE Q4W=80 mg ixekizumab every 4 weeks; ITT=Intent-to-Treat; mTSS=van der Heijde modified Total Sharp Score; NRI=non-responder imputation; PBO=placebo; SD=standard deviation

Baseline Demographics and Disease Characteristics, Extension Period Population

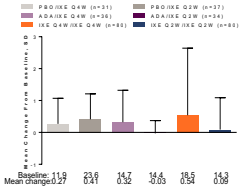
	PBO/ IXE Q4W (N=45)	PBO/ IXE Q2W (N=46)	ADA/ IXE Q4W (N=49)	ADA/ IXE Q2W (N=48)	IXE Q4W/ IXE Q4W (N=97)	IXE Q2W/ IXE Q2W (N=96)
Age, years	50.5 (13.2)	51.0 (11.3)	50.0 (12.6)	46.2 (12.1)	48.7 (10.2)	49.6 (12.8)
Male, n (%)	19 (42.2)	23 (50.0)	21 (42.9)	30 (62.5)	40 (41.2)	44 (45.8)
Time since PsA diagnosis, years	7.9 (7.6)	5.5 (6.5)	7.5 (7.8)	5.9 (5.6)	6.2 (6.5)	7.3 (8.3)
Background cDMARD therapy, n (%)						
Naïve	4 (8.9)	8 (17.4)	8 (16.3)	5 (10.4)	15 (15.5)	16 (16.7)
Past use	15 (33.3)	8 (17.4)	10 (20.4)	9 (18.8)	21 (21.6)	22 (22.9)
Current use	26 (57.8)	30 (65.2)	31 (63.3)	34 (70.8)	61 (62.9)	58 (60.4)
Tender joint count (68 joints)	18.5 (11.6)	19.2 (14.0)	18.8 (11.9)	18.8 (12.8)	20.8 (13.6)	21.3 (13.8)
Swollen joint count (66 joints)	9.6 (6.2)	10.7 (7.1)	10.1 (7.4)	9.6 (5.5)	11.0 (7.3)	12.2 (7.3)
CRP, mg/L	15.4 (29.5)	16.9 (20.4)	12.5 (12.7)	14.4 (24.7)	13.1 (17.0)	15.5 (26.7)
mTSS	**11.5 (15.5)**	**24.5 (37.3)**	**15.6 (24.3)**	**15.4 (30.2)**	**19.6 (33.3)**	**15.2 (29.1)**
Patients with erosions, n/Nx (%)	44/45 (97.8)	45/45 (100.0)	44/48 (91.7%)	46/46 (100.0)	89/96 (92.7%)	92/96 (95.8%)

Data are mean (standard deviation) unless stated otherwise
ADA=40 mg adalimumab every 2 weeks (active reference arm); BMI=body mass index; cDMARD=conventional disease-modifying antirheumatic drug; CRP=C-reactive protein; HAQ-DI=Health Assessment Questionnaire-Disability Index; IXE Q2W=80 ixekizumab every 2 weeks; IXE Q4W=80 mg ixekizumab every 4 weeks; mTSS=van der Heijde modified Total Sharp Score; Nx=number of patients with nonmissing values; PBO=placebo; PsA=psoriatic arthritis

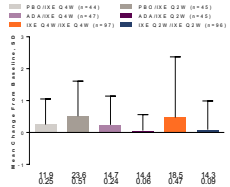
mTSS Change From Baseline to Week 52, Linear Extrapolation, Extension Period Population

- The mTSS change from baseline to Week 52 was minimal for all groups (prespecified and post hoc analysis)

Prespecified Analysis[a] (data after visit excluded)



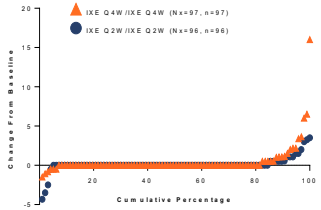
Post Hoc Analysis[b] (data after visit interpolated)



[a]Data were excluded if the radiograph was taken after the scheduled visit date; [b] Data from radiographs taken after the scheduled visit date were interpolated
ADA=40 mg adalimumab every 2 weeks (active reference arm); IXE Q2W=80 ixekizumab every 2 weeks; IXE Q4W=80 mg ixekizumab every 4 weeks; mTSS=van der Heijde modified Total Sharp Score; PBO=placebo; SD=standard deviation

Continuous Ixekizumab Groups: mTSS Individual-Patient Change From Baseline to Week 52 Cumulative Probability Plot, Linear Extrapolation,[a] Extension Period Population

- The majority of patients exhibited either no or minimal structural progression through 52 weeks of treatment with ixekizumab

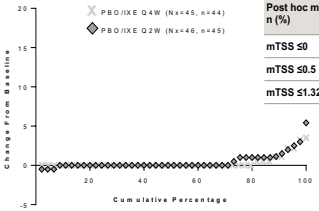


Post hoc mTSS, n (%)	IXE Q4W/ IXE Q4W (Nx=97)	IXE Q2W/ IXE Q2W (Nx=96)
mTSS ≤0	79 (81.4)	81 (84.4)
mTSS ≤0.5	83 (85.6)	86 (89.6)
mTSS ≤1.32 (SDC[c])	88 (90.7)	90 (93.8)

[a] Post hoc analysis: data from radiographs taken after the scheduled visit date were interpolated; [b] 1.32 cut-off based on the SDC from baseline to Week 52 in this study
IXE Q2W=80 ixekizumab every 2 weeks; IXE Q4W=80 mg ixekizumab every 4 weeks; mTSS=van der Heijde modified Total Sharp Score; Nx=number of patients with non-missing change from baseline data; SDC=smallest detectable change

Placebo/Ixekizumab Groups: mTSS Individual-Patient Change From Baseline to Week 52 Cumulative Probability Plot, Linear Extrapolation,[a] Extension Period Population

- On switching from placebo to ixekizumab, the majority of patients exhibited either no or minimal structural progression through 52 weeks of treatment

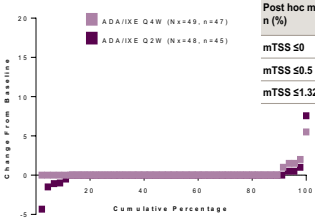


Post hoc mTSS, n (%)	PBO/ IXE Q4W (Nx=44)	PBO/ IXE Q2W (Nx=45)
mTSS ≤0	37 (84.1)	32 (71.1)
mTSS ≤0.5	40 (90.9)	33 (73.3)
mTSS ≤1.32 (SDC[b])	41 (93.2)	40 (88.9)

[a] Post hoc analysis: data from radiographs taken after the scheduled visit date were interpolated; [b] 1.32 cut-off based on he SDC from baseline to Week 52 in this study; IXE Q2W=80 ixekizumab every 2 weeks; IXE Q4W=80 mg ixekizumab every 4 weeks; mTSS=van der Heijde modified Total Sharp Score; Nx=number of patients with non-missing change from baseline data; PBO=placebo; SDC=smallest detectable change

Adalimumab/Ixekizumab Groups: mTSS Individual-Patient Change From Baseline to Week 52 Cumulative Probability Plot, Linear Extrapolation,[a] Extension Period Population

- On switching from adalimumab to ixekizumab, the majority of patients exhibited either no or minimal structural progression through 52 weeks of treatment



Post hoc mTSS, n (%)	ADA/ IXE Q4W (Nx=47)	ADA/ IXE Q2W (Nx=45)
mTSS ≤0	42 (89.4)	41 (91.1)
mTSS ≤0.5	42 (89.4)	43 (95.6)
mTSS ≤1.32 (SDC[c])	43 (91.5)	44 (97.8)

[a] Post hoc analysis: data from radiographs taken after the scheduled visit date were interpolated; b 1.32 cut-off based on the SDC from baseline to Week 52 in this study; ADA=40 mg adalimumab every 2 weeks (active reference arm); IXE Q2W=80 ixekizumab every 2 weeks; IXE Q4W=80 mg ixekizumab every 4 weeks; mTSS=van der Heijde modified Total Sharp Score; Nx=number of patients with non-missing change from baseline data; SDC=smallest detectable change

CONCLUSIONS

- Over a 52-week period, minimal changes in mTSS were observed in patients with psoriatic arthritis who entered the Extension Period and were treated with ixekizumab 80 mg every 2 or 4 weeks

Disclosures

- **D. van der Heijde** is a consultant for: AbbVie, Amgen, Astellas, AstraZeneca, Bristol-Myers Squibb, Boehringer Ingelheim, Celgene, Daiichi-Sankyo, Eli Lilly and Company, Galapagos, Gilead, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, UCB, and Director of Imaging Rheumatology BV;
  M. Okada is a consultant for and has received grant/research support from: Eli Lilly and Company, is on the speaker's bureau of: Santen Pharmaceutical, Mitsubishi Tanabe Pharma, Pfizer, Abbott Japan;
  C. Lee; C. L. Shuler; S. Rathmann; D. Amato and **C-Y. Lin** are current employees and shareholders of: Eli Lilly and Company;
  P. J. Mease is a consultant for and has received grant/research support from: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Crescendo, Eli Lilly and Company, Genentech, Janssen, Merck, Novartis, Pfizer, UCB, is on the speaker's bureau of: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Crescendo, Genentech, Janssen, Pfizer, and UCB
- This study was sponsored by Eli Lilly and Company. Medical writing services were provided by Luke Carey, PhD, of ProScribe – part of the Envision Pharma Group, and were funded by Eli Lilly and Company

Acknowledgments

- The authors would like to thank:
  - All patients who participated in the study
  - All study investigators
  - Justin Grondines and Ingrid Burton from ClinBAY for providing programming support

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Winter Clinical Dermatology Conference – 2018, Kaanapali, HI, USA; January 12-17, 2018; Previously presented at EULAR 2017

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